A spatially dynamic cohort of regulatory genes in the endomesodermal gene network of the sea urchin embryo.

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Public Summary:
During the process of development large cohorts of genes are often activated together in specific patterns, and then it is the action of these gene products that creates new patterns of expression of other genes. Though it is not known to what extent tissue regeneration recapitulates normal developmental processes, it is likely that this basic feature of normal development represents a fundamental element of tissue regeneration as well. Genomics platforms allow us to identify prospectively the genes involved in this process. This marks a significant advance in our ability to “discover” critical genes. We used these instruments to identify a cohort of genes driving early development of the sea urchin embryo. We gained insight into both the mechanisms by which this process works and the methods that will enable novel and penetrating studies of tissue regeneration.

Scientific Abstract:
A gene regulatory network subcircuit comprising the otx, wnt8, and blimp1 genes accounts for a moving torus of gene expression that sweeps concentrically across the vegetal domain of the sea urchin embryo. Here we confirm by mutation the inputs into the blimp1cis-regulatory module predicted by network analysis. Its essential design feature is that it includes both activation and autorepression sites. The wnt8 gene is functionally linked into the subcircuit in that cells receiving this ligand generate a beta-catenin/Tcf input required for blimp1 expression, while the wnt8 gene in turn requires a Blimp1 input. Their torus-like spatial expression patterns and gene regulatory analysis indicate that the genes even-skipped and hox11/13b are also entrained by this subcircuit. We verify the cis-regulatory inputs of even-skipped predicted by network analysis. These include activation by beta-catenin/Tcf and Blimp1, repression within the torus by Hox11/13b, and repression outside the torus by Tcf in the absence of Wnt8 signal input. Thus even-skipped and hox11/13b, along with blimp1 and wnt8, are members of a cohort of torus genes with similar regulatory inputs and similar, though slightly out-of-phase, expression patterns, which reflect differences in cis-regulatory design.